Agency for Healthcare Research and Quality
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NATIONAL GUIDELINE CLEARINGHOUSE

General

Guideline Title

Consensus treatment recommendations for late-onset Pompe disease.

Bibliographic Source(s)

Cupler EJ, Berger KI, Leshner RT, Wolfe GI, Han JJ, Barohn RJ, Kissel JT, AANEM Consensus Committee on Late-onset Pompe Disease. Consensus treatment recommendations for late-onset Pompe disease. Muscle Nerve. 2012 Mar;45(3):319-33. [108 references] PubMed

Guideline Status

This is the current release of the guideline.

Recommendations

Major Recommendations

Treatment Recommendations for the Musculoskeletal Element of Late-Onset Pompe Disease

Provide Patient with Information on the Following Resources

- Muscular Dystrophy Association
- Acid Maltase Deficiency Association
- Pompe Registry
- Association for Glycogen Storage Disease
- International Pompe Association

Physical Examination and Assessments

- Patients should be examined by a cardiologist and pulmonologist before beginning an exercise program.
- Screen all patients diagnosed with Pompe disease, regardless of age and wheelchair use, with dual-energy x-ray absorptiometry (DEXA); follow-ups can be considered on a yearly basis.
- Patients with late-onset Pompe disease and reduced bone density should undergo medical evaluation, including laboratory testing and medication review by an endocrinologist or bone density specialist.
- Conduct fall risk assessment followed by a formal evaluation for balance and safe gait training for patients at increased risk for osteoporosis and falls.
- Recommend adaptive equipment, such as a cane or walker, to reduce risk of falls.

Physical/Occupational Therapy

- A physical or occupational therapist should develop an exercise program that may include one or more of the following: walking, treadmill, cycling, pool-based program, swimming, submaximal aerobic exercise, or muscle strengthening, that follows the guidelines for other degenerative muscle diseases.
- Avoid overwork weakness, excessive fatigue, disuse, strenuous exercises, and eccentric contractions.
- Emphasize submaximal aerobic exercise.
- Incorporate functional activities when possible.
- Teach patient to monitor heart rate and breathing in relation to exertion.
- Integrate energy conservation techniques and biomechanical advantages.
- A preventive stretching regimen should be started early and performed as part of the daily routine to prevent or slow the development of muscle contractures and deformities.

Management of Contractures

- Manage contractures by using orthotic devices, appropriate seating position in the wheelchair, and standing supports.
- Surgical intervention
- Surgical intervention should be considered for scoliosis when the Cobb angle is between 30° and 40°.

Vitamins and Mineral Supplements

- Recommend vitamin D, calcium, and bisphosphonates, following the guidelines for other neuromuscular disorders.

Treatment Recommendations for the Respiratory Element of Late-Onset Pompe Disease

- Involve a pulmonologist experienced in managing patients with neuromuscular diseases.
- Up-to-date vaccinations, including vaccination against pneumococcus and influenza
- Early and aggressive treatment of bacterial and viral infections
- Clear secretions from airways (e.g., cough assist device, suction)
- Train/educate patients and families to use assisted cough and inspiratory muscle techniques.
- Treat sleep-disordered breathing with continuous positive airway pressure (CPAP) or bilevel nocturnal noninvasive ventilation (BiPAP).
- In the absence of sleep studies, consider BiPAP ventilation if arterial Pco_2 is ≥45 mm Hg, supine forced vital capacity is <50% of predicted, negative inspiratory force is <60 cm H_2O, or oxygen saturation falls to <88% for 5 continuous minutes during sleep.
- Treat concomitant conditions, such as asthma or cardiomyopathy.
- Consider enzyme replacement therapy.

Treatment Recommendations for the Gastrointestinal Element of Late-Onset Pompe Disease (Kishnani et al., 2006)

- Coordinate treatment through a multidisciplinary neuromuscular clinic.
- Involve an experienced dietitian.
- Obtain videofluoroscopic swallowing assessment and evaluation for gastroesophageal reflux to guide management of feeding either orally or through a feeding tube.
- Monitor growth parameters carefully.
- Provide adequate nutrition consisting of high protein diet (20% to 25%) with attention to vitamins and minerals.
- Educate patients about the appropriate use of over-the-counter medications.
- Patients receiving enzyme replacement therapy should be monitored for immunoglobulin G (IgG) antibodies every 3 months for 2 years and then annually thereafter.

Treatment Warning for Alglucosidase alfa (Lumizyme; Genzyme Corporation, Cambridge, Massachusetts) ("Lumizyme," 2010)

- *Warning*: Life-threatening anaphylactic reactions, severe allergic reactions, and immune-mediated reactions have been observed in some patients during Lumizyme infusions (van der Ploeg et al., 2010). Therefore, appropriate medical support should be readily available when Lumizyme is administered.

Treatment Recommendations Based on the Stage and Severity of Pompe Disease

Condition	Recommendations
Presymptomatic patients without objective signs	• Patients should be examined every 6 months for proximal muscle weakness and pulmonary function . • Enzyme replacement therapy (ERT) should be started at:

Condition	Recommendations
	• Onset of symptoms • Onset of detectable proximal muscle weakness or reduced forced vital capacity in either upright or supine position
Presymptomatic patients with objective signs	• ERT should be started if: • Presymptomatic patients have proximal muscle weakness detectable on the Medical Research Council scale or reduced forced vital capacity in either upright or supine position

Symptomatic patients	• ERT should be started if:
	  • There is either reduction in forced vital capacity in either upright or supine position or increased limb weakness
	  • Patient has difficulty completing activities of daily living
	  • Is or is not using noninvasive ventilation

Severe symptoms	• If the patient is confined to a wheelchair and is using invasive ventilation during the day and at night:
	  • ERT is recommended for 1 year, followed by evaluation of the effectiveness of therapy.
	  • After one year, ERT is recommended on a case-by-case basis for patients who require continuous invasive ventilation, using the collective information acquired by the multispecialty team.
	  • Continue ERT if severe signs and symptoms are stabilized or improved.

Length of ERT Monitoring	• One year followed by reassessment to consider whether to continue the treatment • Patients receiving enzyme replacement therapy should be monitored for immunoglobulin G (IgG) antibodies every 3 months for 2 years, then annually thereafter.

Treatment Recommendations Based on the Experience in Taiwan (Chien et al., 2009)

- The authors recommend the implementation of newborn screening programs in all states to diagnose and properly treat infants with or at risk of developing infantile-onset or late-onset Pompe disease.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Late-onset Pompe disease

Guideline Category

Evaluation

Management

Rehabilitation

Risk Assessment

Screening

Treatment

Clinical Specialty

Cardiology

Endocrinology

Family Practice

Gastroenterology

Internal Medicine

Medical Genetics

Neurology

Nutrition

Pediatrics

Physical Medicine and Rehabilitation

Pulmonary Medicine

Sleep Medicine

Speech-Language Pathology

Intended Users

Advanced Practice Nurses

Dietitians

Nurses

Occupational Therapists

Physical Therapists

Physicians

Respiratory Care Practitioners

Social Workers

Speech-Language Pathologists

Guideline Objective(s)

To propose consensus-based treatment and management recommendations for late-onset Pompe disease

Target Population

Patients with late-onset Pompe disease

Interventions and Practices Considered

1. Musculoskeletal element of late-onset Pompe disease
    - Providing patients with information on resources related to late-onset Pompe disease
    - Physical examination and assessments

        - Examination by a cardiologist and pulmonologist before beginning an exercise program
        - Screening with dual-energy x-ray absorptiometry (DEXA) with yearly follow-ups
        - Medical evaluation, laboratory testing, and medication review by an endocrinologist or bone density specialist
        - Fall risk assessment, formal evaluation for balance, and safe gait training for patients at increased risk for osteoporosis and falls
        - Adaptive equipment, such as a cane or walker
    - Exercise program developed by a physical or occupational therapist
    - Management of contractures (orthotic devices, surgical interventions)
    - Vitamin D, calcium, and bisphosphonate supplements
2. Respiratory element of late-onset Pompe disease
    - Management by pulmonologist experienced with neuromuscular diseases
    - Up-to-date vaccinations, including vaccination against pneumococcus and influenza
    - Early and aggressive treatment of bacterial and viral infections
    - Clearing secretions from airways (e.g., cough assist device, suction)
    - Training/educating patients and families to use assisted cough and inspiratory muscle techniques
    - Treatment of sleep-disordered breathing with continuous positive airway pressure (CPAP) or bilevel nocturnal noninvasive ventilation (BiPAP)
    - Treatment of concomitant conditions, such as asthma or cardiomyopathy
    - Enzyme replacement therapy (ERT) (alglucosidase alfa [Lumizyme])
        - Initiation of ERT based on symptom assessment
        - Duration of ERT
        - Monitoring ERT for effectiveness and immunoglobulin G (IgG) antibodies
3. Gastrointestinal element of late-onset Pompe disease
    - Coordinating treatment through a multidisciplinary neuromuscular clinic
    - Involving an experienced dietitian in management
    - Videofluoroscopic swallowing assessment and evaluation for gastroesophageal reflux
    - Monitoring growth parameters
    - Providing adequate nutrition consisting of high protein diet, vitamins and minerals
    - Educating patients about the appropriate use of over-the-counter medications
    - Monitoring for IgG antibodies in patients receiving ERT
4. Implementation of newborn screening programs

Major Outcomes Considered

- Pulmonary function
- Muscle strength
- Distance walked during a 6-minute walk test
- Percent of predicted forced vital capacity (FVC) in the upright position
- Quality of life

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

A literature search was conducted in the PubMed and EMBASE databases for clinical trials and relevant articles published before June 2010. The

search terms included *Pompe disease, acid alpha-glucosidase deficiency, acid maltase deficiency, glycogen storage disease type II*, and *glycogenosis type II*. Panel members reviewed these articles individually and discussed them in small group sessions. Subsequently, the panel convened for further discussion and consensus development. In addition, articles published after the consensus meeting was held, references cited by the articles produced by the literature search, and references suggested by the authors are included in this article.

Number of Source Documents

The literature search produced 105 articles relevant to Pompe disease.

Methods Used to Assess the Quality and Strength of the Evidence

Expert Consensus

Rating Scheme for the Strength of the Evidence

Not applicable

Methods Used to Analyze the Evidence

Review

Description of the Methods Used to Analyze the Evidence

Not stated

Methods Used to Formulate the Recommendations

Expert Consensus (Consensus Development Conference)

Description of Methods Used to Formulate the Recommendations

The American Association of Neuromuscular and Electrodiagnostic Medicine (AANEM) convened a consensus committee of specialists with expertise in the diagnosis and treatment of Pompe disease. The AANEM consensus panel, consisting of several neuromuscular specialists and a pulmonologist, reviewed all articles found as a result of the literature search. Each panel member was assigned a section to write and review. Using a modified consensus development conference method, the committee worked to create consensus-based recommendations for the treatment of late-onset Pompe disease.

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

Internal Peer Review

Description of Method of Guideline Validation

The guideline underwent peer review by the Professional Practice Committee and the American Association of Neuromuscular and Electrodiagnostic Medicine (AANEM) Board.

This guideline was approved by the AANEM Board, September 2011.

Evidence Supporting the Recommendations

References Supporting the Recommendations

Chien YH, Lee NC, Thurberg BL, Chiang SC, Zhang XK, Keutzer J, Huang AC, Wu MH, Huang PH, Tsai FJ, Chen YT, Hwu WL. Pompe disease in infants: improving the prognosis by newborn screening and early treatment. Pediatrics. 2009 Dec;124(6):e1116-25. PubMed

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Type of Evidence Supporting the Recommendations

The recommendations are based on expert consensus.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate treatment of late-onset Pompe disease

Potential Harms

- Life-threatening anaphylactic reactions, severe allergic reactions, and immune-mediated reactions have been observed in some patients during Lumizyme infusions. Therefore, appropriate medical support should be readily available when Lumizyme is administered.
- Therapeutic exercise in late-onset Pompe disease may pose a risk for cardiopulmonary compromise in this population. Consequently, a pulmonologist should evaluate the patient before initiation of an exercise program.
- Aggressive stretching should be approached cautiously because, at least in severely affected children, a tendency for pathologic fracture has been observed.

Qualifying Statements

Qualifying Statements

Qualifying Statements

This article was prepared and reviewed by the American Association of Neuromuscular and Electrodiagnostic Medicine (AANEM) and did not undergo the separate review process of Muscle & Nerve.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

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Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2012 Mar

Guideline Developer(s)

American Association of Neuromuscular and Electrodiagnostic Medicine - Medical Specialty Society

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This article was sponsored by an unrestricted grant from Genzyme Corporation.

Guideline Committee

American Association of Neuromuscular and Electrodiagnostic Medicine (AANEM) Consensus Committee on Late-Onset Pompe Disease

AANEM Task Force

Composition of Group That Authored the Guideline

Task Force Members: Edward J. Cupler, MD, Department of Neurology, Oregon Health & Science University, Portland, Oregon, USA; Kenneth I. Berger, MD, Division of Pulmonary and Critical Care Medicine, Department of Medicine and Department of Physiology and Neuroscience, New York University School of Medicine, New York, New York, USA; Robert T. Leshner, MD, Department of Neurosciences, University of California San Diego, San Diego, California, USA; Gil I. Wolfe, MD, Department of Neurology, University of Texas Southwestern Medical School, Dallas, Texas, USA; Jay J. Han, MD, Department of Physical Medicine and Rehabilitation, University of California Davis, Sacramento, California, USA; Richard J. Barohn, MD (*Co-chair*), Department of Neurology, University of Kansas Medical Center, Kansas City, Kansas, USA; John T. Kissel, MD (*Co-chair*), Department of Neurology, Division of Neuromuscular Medicine, Ohio State University, Columbus, Ohio, USA

Financial Disclosures/Conflicts of Interest

Task Force Co-chairs: Dr. Barohn has nothing to disclose. Dr. Kissel serves as a consultant for Alexion Pharmaceuticals for a clinical trial in myasthenia gravis.

Task Force Members: Dr. Han has nothing to disclose. Dr. Berger has served as a consultant to Genzyme Corporation for clinical trials in MPS I and Pompe disease, and he has served as a consultant to BioMarin Corporation for clinical trials in MPS IV and MPS VI. Dr. Cupler is a member of the speaker bureau for Genzyme Corporation and for Athena Diagnostics, Inc., and is a member of the Pompe Registry North American Board of Advisors for Genzyme Corporation. Dr. Leshner is a member of the Genzyme Global Advisory Board for Pompe disease and has received honoraria for speaking engagements and research support from Genzyme Corporation. Dr. Wolfe has served on the speaker bureau for Genzyme Corporation. None of the authors of this article is an inventor, and no authors are receiving royalty payments. All authors received travel support and honoraria for the initial consensus development meeting from MedLogix Communications, LLC, and the AANEM, through an educational grant from Genzyme Corporation.

Dr. Barohn and Dr. Kissel were the co-chairs of the task force. They were chosen as chairs because they were free from any conflict. Every attempt was made to include authors without a conflict. Due to several physicians being unable to attend the initial meeting, the final panel involved three physicians without a conflict and four with a conflict (KIB, EJC, TRL, GIW).

Guideline Status

This is the current release of the guideline.

Guideline Availability

Electronic copies: Available in Portable Document Format (PDF) from the American Association of Neuromuscular and Electrodiagnostic Medicine (AANEM) Web site .

Availability of Companion Documents

None available

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI Institute on September 14, 2012. The information was verified by the guideline developer on October 29, 2012.

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